UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,259	11/06/2006	Edwin Pei Yong Chow	6565-76130-01	2433

24197 7590 07/14/2009

KLARQUIST SPARKMAN, LLP
121 SW SALMON STREET
SUITE 1600
PORTLAND, OR 97204

EXAMINER	
BECKHARDT, LYNDSEY MARIE	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
07/14/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,259	CHOW ET AL.	
	Examiner	Art Unit	
	LYNDSEY BECKHARDT	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *16-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :03/04/2009, 12/16/2008, 09/11/2008, 02/14/2008, 12/08/2006, 11/06/2006, 06/30/2006.

DETAILED ACTION

Claims 1-24 are currently pending. Claims 1-15 are currently under examination.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-15, in the reply filed on 06/19/2009 is acknowledged. The traversal is on the ground(s) that the Jeong reference does not disclose or suggest that the pores are interconnected and there is no suggestion of Jeong's use of a biocontinuous microemulsion. This has been found persuasive. Jeong does mention porous matrix type drug delivery system; however interconnected pores are not mentioned. Applicant is reminded that the special technical feature does not include a bicontinuous emulsion. In response to applicant's arguments, new prior art is being applied to the special technical feature. The special technical feature is a porous polymer, said polymer defining interconnected pores with a drug dispersed inside said pores and capable of being released. The porous polymer with said drug dispersed in said pores, capable of being released does not present a contribution over the prior art. As disclosed in Chieng et al (Morphology of microporous polymeric materials by polymerization of methyl methacrylate and 2-hydroxyethyl methacrylate in microemulsions, publication date: 1995) in view of Simamora (Controlled delivery of pilocarpine, publication date: 1998) the special technical feature is not novel.

Chieng teaches microemulsions are thermodynamically stable, transparent, isotropic liquids consisting of water and oil phases stabilized by a surfactant or a combination of

surfactant and co surfactant. The phase behaviors of the microemulsion was evaluated, and it was determined that a bicontinuous region was present in the microemulsion (page 1942, second column, first paragraph). A substantial increase in conductivity can be seen as the water content is increased from about 20% to 80%. This is attributed to the presence of biocontinuous structure in which both water and oil domains are interconnected with each other formed conducting channels (page 1943, first column, first paragraph). A continuous increase in viscosity is observed in the microemulsions on increasing the water content up to about 80%. This is because the number of droplets or channels increases on increasing water content which in turn increases the interactions between them (page 1943, first column, second paragraph). The microstructure became very distinctive for samples containing more than 20wt% water. For instance globular microstructure with the dimension of micrometers was seen. They stacked onto each other and the voids (pores) formed resembled the packing of a chromatographic column using fine particle materials. It is believed that these pores were interconnected and were water-filled spaces generated between the incompletely coalesced spherical aggregates (page 1943, column 2, second paragraph). These pores might be derived from water domains of the polymerized microemulsion system (page 1945, first paragraph).

Chieng does not teach the inclusion of a drug dispersed in at least said polymer matrix and releasable therefrom.

Simamora teaches an ocular device for the controlled delivery of pilocarpine was evaluated. The device was fabricated using Gelfoam (absorbably gelatin sponge) in the

form of a matrix system. The gelfoam device is more effective than the two conventional pilocarpine dosage forms in prolonging the duration of the pilocarpine activity (abstract). Most ophthalmic drugs are administered topically in the form of eye drops. Although convenient and inexpensive, this type of deliver system yields low therapeutic efficacy due to the dynamics of the lachrymal system (i.e. blinking, etc). This required more frequent administration and increases the systemic side effects. Therefore, it is necessary to develop safer, efficacious and more acceptable ocular delivery systems. Delivery systems that are capable of releasing the drug in a prolonged manner are of interest because they can improve the ocular residence time (page 209, first paragraph). Ocular inserts that are non-biodegradable, such as Ocuset are known (page 210, second paragraph). Fabrication of a bioerodible eye insert in the form of a matrix system for the controlled delivery of pilocarpine was taught. Commercially available Gelfoam was utilized as the drug carrier. It was found that the embedment of the Gelfoam pores with certain type of retardant is an effective way of controlling drug release without altering the biodegradability (page 210, third paragraph).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the porous polymer taught by Chieng and inset ocular drugs in the pores because ocular implants with pores containing drugs for controlled delivery are known in the art and have many advantages such as less frequent administration and lower side effects as taught by Simamora.

As disclosed in Chieng in view of Simamora, a porous polymer containing interconnected pores with a drug dispersed inside said pores and capable of being released of instant claim 17 is not novel. As such, Group II does not share a special technical feature with the instant claims of Group I and III. Therefore the claims are not so linked within the meaning of PCT Rule 13.2 so as to form a single inventive concept and unity between Groups I-III is broken.

Claims 16-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 06/19/2009.

Priority

This application claims priority to PCT application PCT/SG04/00237, filed 08/04/2004. The effective filing date of the instant application is deemed to be 08/04/2004.

Information Disclosure Statement

Applicant's Informational Disclosure Statements, filed on 06/30/2006, 11/06/2006, 12/08/2006, 02/14/2008, 09/11/2008, 12/16/2008, 03/04/2009, have been considered. Please refer to Applicant's copy of the 1449 submitted herein.

Claim Objections

Claims 6, 9 and 15 objected to because of the following informalities: Abbreviations are recited in claims 6, 9 and 15 without being defined previously in the claim set. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 and 10-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chieng et al (Morphology of microporous polymeric materials by polymerization of methyl methacrylate and 2-hydroxyethyl methacrylate in microemulsions, publication date: 1995) in view of Simamora (Controlled delivery of pilocarpine, publication date: 1998) and Lui (Nanostructured Polymeric Materials from Microemulsion Polymerization Using poly(ethylene oxide) Macromonomer, publication date: 1997).

Chieng teaches microemulsions are thermodynamically stable, transparent, isotropic liquids consisting of water and oil phases stabilized by a surfactant or a combination of surfactant and co surfactant. The microstructure of a microemulsion depends on the composition of the system, one such structure being bicontinuous at intermediate water content. Bicontinuous structure of microemulsions has been extensively investigated. Recently an increase in interest has emerged in studying the formation of porous polymeric solids by polymerization of monomer-containing microemulsions with bicontinuous structures (page 1941, first column, first paragraph). Materials used were methyl methacrylate (MMA), 2-hydroxyethyl methacrylate (HEMA) and ethylene glycol dimethacrylate (EGDMA). Dibenzyl ketone (DBK), sodium dodecylsulfate and dionized water were also used (page 1941, second column, first paragraph). A stock solution containing 20% SDS in water was prepared. The single-phase region of the microemulsion was determined visually by titrating a specific

amount of MMA, HEMA and EGDMA with the stock solution (page 1941, second column, second paragraph). The composition contents in wt% are listed in Table 1 below.

Table 1 Microemulsion compositions used for polymerization[a]

Microemulsion system	Compositions (wt%)				Appearance of the system[b]	
	MMA	HEMA	SDS	Water	BP	AP
H4	57	38	1	4	C	C
H8	54	36	2	8	C	C
H12	51	34	3	12	C	C
H16	48	32	4	16	C	WY
H24	42	28	6	24	C	O
H32	36	24	8	32	C	O
H40	30	20	10	40	C	O
S14	36	24	14	26	C	O
MH55	30	30	8	32	C	O
MH37	18	42	8	32	C	WY
MH19	6	54	8	32	C	WY

[a]Weight ratio of MMA:HEMA was fixed at 3/2 for systems H4, H8, H12, H16, H24, H32, H40 and S14, while that for systems MH55, MH37 and MH19 varied from 5/5 to 3/7 and 1/9 respectively. EGDMA added was 4 wt% based on the total weight of MMA and HEMA, and photoinitiator DBK added was 0.3 wt% based on the total weight of each microemulsion sample
[b]BP = before polymerization; AP = after polymerization; C = clear; WY = white yellowish; O = opaque

(Table 1, page 1942)

The photoinitiator, DBK, was used for initiating the microemulsion polymerization (page 1942, first column, first paragraph).The phase behaviors of the microemulsion was evaluated, and it was determined that a bicontinuous region was present in the microemulsion (page 1942, second column, first paragraph). A substantial increase in conductivity can be seen as the water content is increased from about 20% to 80%. This is attributed to the presence of biocontinuous structure in which both water an oil

domains are interconnected with each other formed conducting channels (page 1943, first column, first paragraph). A continuous increase in viscosity is observed in the microemulsions on increasing the water content up to about 80%. This is because the number of droplets or channels increases on increasing water content which in turn increases the interactions between them (page 1943, first column, second paragraph). The microstructure became very distinctive for samples containing more than 20wt% water. For instance globular microstructure with the dimension of micrometers was seen. They stacked onto each other and the voids (pores) formed resembled the packing of a chromatographic column using fine particle materials. It is believed that these pores were interconnected and were water-filled spaces generated between the incompletely coalesced spherical aggregates (page 1943, column 2, second paragraph). Pores nearly round in shape of dimension ca 1-10um can clearly be seen in SEM micrograph. These pores might be derived from water domains of the polymerized microemulsion system (page 1945, first paragraph).

Chieng does not teach the inclusion of a drug dispersed in at least said polymer matrix and releasable therefrom, wherein said drug is an ophthalmic drug.

Simamora teaches an ocular device for the controlled delivery of pilocarpine was evaluated. The device was fabricated using Gelfoam (absorbably gelatin sponge) in the form of a matrix system. The gelfoam device is more effective than the two conventional pilocarpine dosage forms in prolonging the duration of the pilocarpine activity (abstract). Most ophthalmic drugs are administered topically in the form of eye drops. Although convenient and inexpensive, this type of deliver system yields low

therapeutic efficacy due to the dynamics of the lachrymal system (i.e. blinking, etc). This required more frequent administration and increases the systemic side effects. Therefore, it is necessary to develop safer, efficacious and more acceptable ocular delivery systems. Delivery systems that are capable of released the drug in a prolonged manner are of interest because they can improve the ocular residence time (page 209, first paragraph).Ocular inserts that are non-biodegradable, such as Ocuset are known (page 210, second paragraph). Fabrication of a bioerodible eye insert in the form of a matrix system for the controlled delivery of pilocarpine was taught. Commercially available Gelfoam was utilized as the drug carrier. It was found that the embedment of the Gelfoam pores with certain type of retardant is an effective way of controlling drug release without altering the biodegradability (page 210, third paragraph).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the porous polymer taught by Chieng and inset ocular drugs in the pores because ocular implants with pores containing drugs for controlled delivery are known in the art and have many advantages such as less frequent administration and lower side effects as taught by Simamora.

Liu teaches a transparent nanostructure polymeric materials have been produced from the direct polymerization of bicontinuous microemulsions using the macromonomer ω methoxy poly(ethylene oxide)$_{40}$ undecyl α methacrylate (C1-PEO-C11-MA-40) as a polymerizable nonionic surfactant. Besides the PEO macromonomer, the system also consisted of (MMA), (HEMA), EGDMA and water. The pore size of these transparent

polymeric materials ranges from about 1 to 10 nm in diameter. The PEG filtration provide the direct evidence that bicontinuous nanostructured polymeric materials can be readily prepared via the polymerization of these nonionic bicontinuous miroemulsions (abstract). The amphiphilic PEO macromonomers can undergo a fast micellar polymerization in water (page 6421, first column, first paragraph).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use C1-PEO-C11-MA-40, a non ionic surfactant, as taught by Liu for the surfactant used in the porous microemulsion taught by Chieng because the C1-PEO-C11-MA-40 non ionic surfactant can undergo a fast micellar polymerization in water as taught by Liu. One would have a reasonable expectation of success because the emulsions taught by Lui and Chieng both contain MMA, HEMA and EGDMA, with the only substitution being the surfactant used in Chieng for the C1-PEO-C11-MA-40 surfactant recited by Liu.

In regard to claim 1, the limitations of a bicontinuous microemulsion comprising water, a monomer and a surfactant copolymerized with said monomer to form a porous polymer with interconnected pores filled by water would be obvious over the single-phase region of the microemulsion was determined visually by titrating a specific amount of MMA, HEMA and EGDMA with the stock solution (page 1941, second column, second paragraph). The phase behaviors of the microemulsion was evaluated, and it was determined that a bicontinuous region was present in the microemulsion (page 1942, second column, first paragraph). For instance globular microstructure with

the dimension of micrometers was seen. They stacked onto each other and the voids (pores) formed resembled the packing of a chromatographic column using fine particle materials. It is believed that these pores were interconnected and were water-filled spaces generated between the incompletely coalesced spherical aggregates taught by Chieng (page 1943, column 2, second paragraph). The limitation of a drug dispersed in at least said polymer matrix and releasable therefrom when said porous polymer is in contact with a liquid would be obvious over an ocular device for the controlled deliver of prilocarpine being evaluated (abstract). The ocular device is made of Gelfoam which contains pores in which the drug is embedded as taught by Simamora (page 210, first column, third paragraph). The drug is taught to be released in a controlled manner, and so would be released when placed in contact with the fluid of the eye. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use an ophthalmic drug in the porous microemulsion taught by Chieng because ophthalmic implants for releasing drugs containing pores is well known and has been shown to have several advantages.

Regarding claim 2, the limitation of the drug being ophthalmic would be obvious over an ocular device for controlled delivery of pilocarpine taught by Simamora (abstract).

Regarding claim 3, the limitation of the pores having a diameter of 10 to 100 nm would be obvious over the pore size ranges from about 1 to 10 nm as taught Lui (abstract).

Regarding claim 4, the limitation of water being present from 15-50%, monomer present from 5-40% and surfactant present from 10-50% would be obvious over the compositions used as found in table 1. MMA is present from 6-57%, HEMA is present from 20-54%, SDS is present from 1-14% and water is present from 4-40% as taught by Chieng (page 1942, table 1). The water and surfactant ranges taught by Chieng are within the ranges required by the instant claim. Each monomer by itself would be within the range required form said monomer recited in the instant claim. The combination of the MMA and HEMA monomers would total 60%, which is outside the 40% taught in the instant claims. Use of the about language however allows for additional polymer present outside the exact recited 40%, in which 60% would be included. There is also routine optimization of ranges through standard experimentation. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Regarding claims 5 and 6, the limitation of microemulsion further comprising a cross-linker, wherein the cross linker is EGDMA would be obvious over the inclusion of EGDMA in the formation of the microemulsion as taught by Chieng (page 1941, column 2, paragraphs 1 and 2).

Regarding claims 7 and 8, the limitation of the microemulsion comprising a polymerization initiator, wherein said initiator is a photo-initiator would be obvious over the photoinitiator, DBK, was used for initiating the microemulsion polymerization taught by Chieng (page 1942, first paragraph).

Regarding claim 10, the limitation of polymerizing comprises subjecting said microemulsion to ultraviolet radiation would be obvious over the reactor chamber operated at a wavelength of 235.7 nm as taught by Chieng (page 1942, first paragraph).

Regarding claims 11 and 12, the limitation of the monomer being ethylenically unsaturated, wherein the monomer is methyl methacrylate, 2-hydroxyethyl methacrylate or a combination would be obvious over the microemulsion compositions taught by Table 1, in which MMA and HEMA are both present as taught by Chieng (page 1942, table 1).

Regarding claims 13-15, the limitations of a surfactant being a non-ionic, being poly(ethylene oxide)-macromonomer, and wherein the surfactant is C1-PEO-C11-MA-40 would be obvious over the bicontinuous microemulsion using the macromonomer C1-PEO-C11-MA-40 as a polymerizable nonionic surfactant as taught by Liu (abstract).

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chieng et al (publication date: 1995), Simamora (publication date: 1998) and Lui (publication date: 1997) as applied to claims 1-8 and 10-15 above, and further in view of Havermeyer et al. (Absorption changes under UV illumination in doped PMMA, publication date: 10/05/2000).

As mentioned in the above 103(a) rejection, all the limitations of claims 1-8 and 10-15 are taught by the combination of Chieng, Simamora and Lui. The combination of

references does not teach DMPA (2,2-dimethoxy-2-phenylacetophenone) as the photoinitiator.

Havermeyer teaches poly(methyl methacrylate) (PMMA) containing residual monomer and doped with the photoinitiator 2,2-dimethoxy-2-phenylacetophenone (DMPA) is a photosensitive system for light in the ultraviolet (UV) range. In illuminated regions DMPA molecules decay into free radicals and trigger polymerization reactions of the residual monomer. The light generated free radicals induce polymerization (page 201, first column, first paragraph). This meets the limitations of claim 9.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use DMPA as the photoinitiator as taught by Havermeyer in the microemulsion taught by the combination of Chieng, Simamora and Lui because DMPA is a UV activated photoinitiator capable of polymerizing methacrylate as taught by Havermeyer and the microemulsion taught by the combination of Chieng, Simamora and Lui uses a photoinitiator that is UV activated to polymerize acrylates. One would have a reasonable expectation of success in substituting one UV activated photoinitiator for another UV activated photoinitiator.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LYNDSEY BECKHARDT whose telephone number is

(571)270-7676. The examiner can normally be reached on Monday thru Thursday 7:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571)272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LMB

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615